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PubMed☐ 1: Am J Med Genet 2002 Jan 8;114(1):31-3

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## **Lack of association between cathepsin D genetic polymorphism and Alzheimer disease in a Spanish sample.**

**Mateo I, Sanchez-Guerra M, Combarros O, Llorca J, Infante J, Gonzalez-Garcia J, del Molino JP, Berciano J.**

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Neurology Service, Marques de Valdecilla University Hospital, Santander Spain.

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Cathepsin D (catD) is an intracellular aspartyl protease that exhibits beta and gamma secretase-like activity to cleave amyloid precursor protein into beta amyloid peptide. The T-allele of a biallelic (alleles C and T) polymorphism in the exon 2 of the catD gene has been found to be associated with increased risk of Alzheimer disease (AD) in two independent German populations. Other groups have been unable to replicate this association in Caucasian American and Northern Ireland populations. Moreover, a small and no significant tendency for the T-allele to be protective for AD has been demonstrated in Caribbean Hispanics. A case control study utilizing a clinically well-defined group of 311 sporadic AD patients and 346 control subjects was performed to test this association in an ethnically homogeneous population from Spain. We did not observe any association between the T-allele of the catD gene and the disease. Furthermore, catD was not predictive of AD in an interactive fashion when considering apolipoprotein E, age, or gender. Copyright 2001 Wiley-Liss Inc.

PMID: 11840502 [PubMed - indexed for MEDLINE]

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☐ 1: Neurosci Lett 2000 Jul 28;289(1):61-5

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## The genetic association between Cathepsin D and Alzheimer's disease.

**Crawford FC, Freeman MJ, Schinka J, Abdullah LI, Richards D, Sevush S, Duara R, Mullan MJ.**

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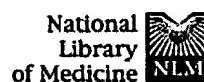
Roskamp Institute and the University of South Florida Memory Disorder Clinic, 3515 E. Fletcher Avenue, Tampa, FL 33613, USA.

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The aspartyl protease Cathepsin D has previously been suggested to play role in the Alzheimer's disease (AD) process because of its ability to cleave the beta-amyloid precursor protein and the possibility that it may be one of the 'secretase' enzymes. A functional C-->T polymorphism in the Cathepsin D gene (CATD) has been reported to be associated with increased risk for AD in Caucasian case-control studies; specifically, the T-carrying genotypes confer increased risk. We have examined this association in our own Caucasian dataset of 210 AD cases and 120 controls, and in an additional Hispanic dataset comprising 79 AD cases and 112 controls. In Hispanics we find a modest interaction between CATD genotype and age at onset on risk for AD, such that the non-T-carrying genotype confers increased risk. In our Caucasian dataset we find no evidence for association between the CATD polymorphism and AD, although we do observe a small tendency towards an increase in the T-carrying genotypes in the case group, consistent with previous studies. We conducted an aggregate analysis of the published Caucasian datasets and found evidence that this CATD polymorphism (or another locus in linkage disequilibrium) does contribute significant, but small (<2%) risk for AD.

### Publication Types:

- Clinical Trial
- Multicenter Study
- Randomized Controlled Trial



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1: Am J Med Genet 2001 Mar 8;105(2):179-82

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## Non-replication of association between cathepsin D genotype and late onset Alzheimer disease.

Menzer G, Muller-Thomsen T, Meins W, Alberici A, Binetti G, Hock C, Nitsch RM, Stoppe G, Reiss J, Finckh U.

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Department of Human Genetics, University Hospital Hamburg-Eppendorf Germany.

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In two recent studies from Germany, a strong association was found between the allelic variant T of the amino acid substitution encoding polymorphism 224 C/T (A38V) in exon 2 of the cathepsin D gene (CTSD) and late onset Alzheimer disease (AD). Other studies from Europe and the USA revealed ambiguous results. Therefore, we performed an independent association study on CTSD and AD in a sample of 324 Caucasian patients from Germany, Switzerland, and Italy with late onset AD, and 302 non-demented controls. We could not confirm an association between CTSD genotype and AD, although there was a slight but not significant increase in frequency of the T allele and T carrier status in AD. Post hoc data analyses suggested that there might be a stronger effect of CTSD genotype on AD risk in males, and an interaction between CTSD and APOE genotypes in males but not females. Copyright 2001 Wiley-Liss, Inc.

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1: Ann Neurol 2001 Apr;49(4):544-5

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- [Ann Neurol. 2000 Mar;47\(3\):399-403.](#)

## Cathepsin D polymorphism not associated with Alzheimer's disease in Japanese.

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Matsui T, Morikawa Y, Tojo M, Okamura N, Maruyama M, Hirai F, Chiba H, Matsushita S, Higuchi S, Arai H, Sasaki H.

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